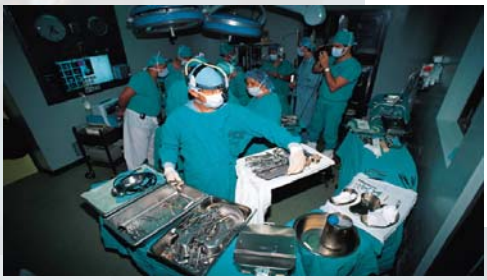
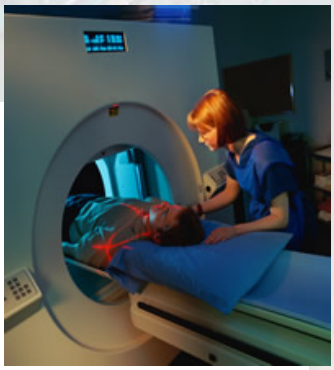
C·D·R·H
Center for Devices and Radiological Health



2005 CDRH FY 2005 Highlights

Reporting for the period between
October 1, 2004 and September 30, 2005



United States Department of Health & Human Services

Center for Devices and Radiological Health
CDRH

FDA

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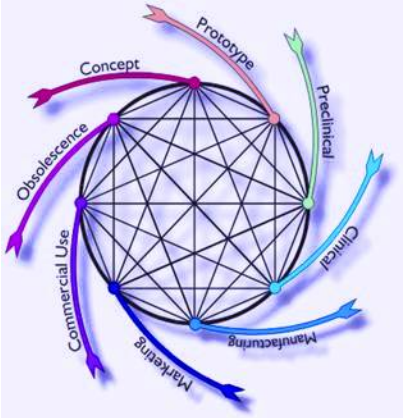


CDRH

Promoting and protecting public health by ensuring the safety and effectiveness of medical devices and the safety of radiological products

Ensuring the health of the public throughout the Total Product Life Cycle

www.FDA.Gov/CDRH

MESSAGE FROM THE CENTER DIRECTOR

Dear Reader,

I'm pleased to issue the annual report for FDA's Center for Devices and Radiological Health, which highlights both the challenges we faced and the goals we met during Fiscal Year 2005. This letter briefly summarizes some of the major accomplishments described in the report. I encourage you to visit CDRH's web site at www.fda.gov/cdrh to read the full report and learn more about what we do.

FY 2005 was the first year that the majority of MDUFMA performance goals went into effect. I'm pleased to report that hard work and preparation paid off—we not only fulfilled MDUFMA requirements, but maintained device review performance in areas not covered by MDUFMA. And we're now in the process of preparing for MDUFMA II.

Seventy percent of our resources were related to MDUFMA activities in FY2005. This involved all aspects of the review process, including condition of approval studies, statistical review, human factors review, labeling review, research and consultation, review of manufacturing practices, pre-approval inspections and third party inspections.

With MDUFMA, we are making significant strides in our premarket programs. But our responsibility to public health goes beyond premarket review. We also need to transform our postmarket program to better monitor the safety of medical devices after they reach the market. This year we took a major first step in that direction with a comprehensive, year-long internal inventory of the tools used to monitor the safety of medical devices after they are in use. The inventory identified areas where we are performing well, as well as those where we need to improve. With the inventory as a roadmap, we will take steps to enhance our ability to identify, analyze, and act on problems quickly, so that we can better alert patients and health professionals about medical device safety issues.

In order to get our medical device safety messages to the people who need them, we must have an effective communications system that will link us with clinicians, medical institutions, patients and the general public. To help satisfy that need, we began a systematic review of our medical device websites to enhance our information on product safety and to make our web pages more accessible and user-friendly. We began research to determine whether our safety messages meet the needs of patients and the healthcare community. I'm also pleased to report that "FDA Patient Safety News," our video news show for health professionals, continues to attract new viewers, with a 40 percent increase in visitors to the show's dedicated website in FY 2005.

Medical device technology is moving forward at incredible speed, and our internal research programs help us keep pace with emerging science. They make an important

contribution to our product review process, and help stimulate the development of new evaluation tools. For example, CDRH scientists conducted research in 2005 that aided in the evaluation of a post-approval study application for a pediatric left ventricular assist device (LVAD).

In an age of rapid scientific and medical progress, it is vital that we strengthen our interactions with the academic and clinical communities. Our Medical Device Fellowship Program continues to attract outside experts to work with us on a short-term basis, sharing their expertise and gaining insight into our policies and public health mission. At the same time, the Center's Staff College helps to assure that the knowledge and qualifications of our own staff are continually enhanced.

In FY 2005 CDRH commemorated 10 years of Mammography Quality Standards Act inspections. In that decade, MQSA inspectors have completed 93,000 inspections of mammography facilities. I'm pleased to note that the percentage of inspections without adverse observations has increased, and continues to do so. In FY 2005 we also published amendments to the mandatory medical x-ray performance standards that should significantly reduce patient radiation exposure from fluoroscopy.

We were presented with an unusual challenge in FY 2005 because of Hurricane Katrina. We responded quickly by issuing advice on the disposal of contaminated devices, the reopening of dialysis centers, and how to deal with medical devices that have been exposed to high heat and humidity and those that require refrigeration. I am especially proud of all of the volunteers in the Center who traveled to New Orleans and other hard-hit areas to help in the recovery effort.

To sum up, I'm proud of our accomplishments, but I'm also aware of the challenges that lie ahead: improving the efficiency and quality of our premarket review system, strengthening our postmarket program to provide a strong public health safety net for products already in use, focusing our research program to better address emerging regulatory issues, communicating more effectively within the Center, with healthcare professionals, patients and the medical device industry, improving our lines of communication with the academic and clinical communities, and assuring that our own staff is adequately trained to deal with the challenging new technologies on the horizon.

None of the progress outlined in this letter could have occurred without the commitment and hard work of everyone in the Center. I'm proud of them and grateful for their dedication to the public health.

Daniel G. Schultz, M.D.
Director, Center for Devices and
Radiological Health

INCREASING ACCESS TO INNOVATIVE TECHNOLOGIES

ENABLING TECHNOLOGY AND INNOVATION

The following devices are examples of advanced device technologies that FDA approved or cleared during FY 2005. A comprehensive list of approved medical devices is available at http://www.fda.gov/cdrh/consumer/mda/index.html.

MINIMALLY INVASIVE SURGERY
http://www.fda.gov/cdrh/mda/docs/p040003.html
The ExAblate 2000 System, manufactured by InSightec, is the first non-invasive surgery device to combine magnetic resonance imaging and focused ultrasound to target and destroy uterine fibroids. The device is intended to treat women who have completed childbearing or do not intend to become pregnant. It is an alternative to myomectomy, hysterectomy, watchful waiting, hormone therapy, or uterine fibroid embolization.

ORAL RINSE FOR GINGIVITIS
http://www.fda.gov/cdrh/mda/docs/k041482.html
The Decapinol Oral Rinse, manufactured by Sinclair Pharmaceuticals Limited, is a prescription oral rinse. When used, the oral rinse forms a physical barrier to bacterial attachment on tooth surfaces. The interference to bacterial attachment reduces plaque associated with gingivitis.

SURGICAL LASER FOR ASSISTED REPRODUCTION
http://www.fda.gov/cdrh/mda/docs/k040045.html
The Hamilton Thorne Zona Infrared Laser Optical System (ZILOS-tk®), manufactured by Hamilton Thorne Biosciences, Inc., is a microscope guided laser system used to drill a small hole in the zona pellucida, the hard membrane that surrounds the ovum, and facilitate embryo hatching prior to implantation. The device may increase implantation rates in older women (older than 37 years) and patients utilizing frozen embryos.

INCREASING ACCESS TO INNOVATIVE TECHNOLOGIES

TREATING ANEURYSMS OF THE THORACIC AORTA
http://www.fda.gov/cdrh/mda/docs/p040043.html
The GORE TAG Endoprosthesis System, manufactured by W.L. Gore and Associates, Inc., is the first endovascular grafting system approved to treat aneurysms of the descending thoracic aorta (in the chest). The device is intended to prevent aneurysm ruptures by making a new path for blood flow. The GORE TAG Endoprosthesis can be used instead of more invasive open surgery to repair the aorta, the main artery that carries blood in the body.

DURA MATER SEALANT FOR NEUROSURGERY
http://www.fda.gov/cdrh/mda/docs/p040034.html
The DuraSeal Dural Sealant System, manufactured by Confluent Surgical, Inc., is the first material approved for sealing leaks in the dura mater covering of the brain during neurosurgical procedures. The sealant is intended to aid in preventing cerebrospinal fluid leakage through suture wound edges of the dura mater is absorbable and will biodegrade within 4-8 weeks after application.

DRUG-ELUTING PACEMAKER LEAD RELEASING STEROID TO IMPROVE HEALING
http://www.fda.gov/cdrh/mda/docs/p030036.html
The SelectSecure™ Lead Model 3830, manufactured by Medtronic, Inc., is a surgically implanted wire that connects the heart to an implanted pacemaker. A steroid, beclomethasone dipropionate, is released into the body from the tip of the lead to improve healing after implantation. The lead, in conjunction with an implanted pacemaker, treats irregular or slow heart rhythm or bradycardia. If bradycardia is not treated, it can lead to fatigue, shortness of breath, dizziness, or fainting.

NEW PROSTHETIC JAW JOINT
http://www.fda.gov/cdrh/mda/docs/p020016.html
The Total Temporomandibular Joint Replacement System, manufactured by Walter Lorenz Surgical, Inc., is a prosthetic jaw joint intended for patients who need a total jaw replacement due to severe arthritic conditions, fused joints, previous multiple surgeries, severe fractures, tumors, or severely degenerated joints. The device may reduce jaw pain, reduce interference with eating and increase the ability to open the mouth.

FIRST DNA-BASED TEST FOR A DRUG METABOLIZING ENZYME
http://www.fda.gov/cdrh/pdf5/K051824.pdf
The Invader® UGT1A1 Molecular Assay, manufactured by Third Wave Technologies, Inc., is intended to help doctors make personalized drug treatment decisions. This assay

enables doctors to use a patient's genetic information for determining whether to modify the dose for drugs that are broken down in the body by UGT enzymes. Drug dose modification could minimize harmful drug reactions and prevent patients from being improperly treated with suboptimal doses. The Invader assay joined a growing list of DNA-based tests used for individualized medical care.

NEW TECHNOLOGY FOR MAINTAINING PATIENT DATA
http://www.fda.gov/cdrh/pdf3/k033440.pdf
The VeriChip Implantable Radiofrequency Transponder System, manufactured by Applied Digital Solutions, consists of an implantable chip, an introducer, and a reader. After the chip is implanted under the skin, a caregiver is able to retrieve a unique patient identifier and patient medical information from a prescription web site when the patient is otherwise unable to provide this information. The medical information on the web site is supplied by the patient and can only be accessed with appropriate authorization.

THE FIRST SURGICAL MARKER WITH RFID TECHNOLOGY
http://www.fda.gov/cdrh/pdf4/k042555.pdf
The SurgiChip Tag Surgical Marker system, manufactured by SurgiChip Inc., is the first surgical marker to use radio frequency identification (RFID) technology to mark an anatomical site for surgery. This external surgical marker tag is intended to lessen the likelihood of wrong-site, wrong-procedure and wrong-patient surgeries.

PREVENTION OF FUTURE STROKES
http://www.fda.gov/cdrh/mda/docs/p040038.html
The Xact® Carotid Stent System, manufactured by Abbott Vascular Devices, is used to open blood vessels in patients who have had a stroke, who have a very tight blockage in the vessels of the neck, and who have counter indications for the surgical alternative. The device, a mesh stent with delivery catheter (Xact® Carotid Stent System), is used in combination with a micromesh filter basket on a catheter to trap loose debris particles (Emboshield Embolic Protection System).

ARTIFICIAL INTERVERTEBRAL DISC
http://www.fda.gov/cdrh/mda/docs/p040006.html
The CHARITE™ Artificial Disc, manufactured by DePuy Spine, Inc, is indicated for use in spinal reconstruction in patients with degenerative disc disease. The device consists of an artificial intervertebral disc of metal and plastic that is surgically implanted to replace a diseased or damaged intervertebral disc. The

artificial disc may restore disc height, reduce pain, and allow movement at the level where it is implanted.

PROVIDING CIRCULATORY SUPPORT FOR HOSPITALIZED PATIENTS AWAITING HEART TRANSPLANTATION
http://www.fda.gov/cdrh/mda/docs/p030011.html
The Syncardia Temporary CardioWest Total Artificial Heart (TAH-t), manufactured by SynCardia Systems, Inc., is indicated for use in heart transplant-eligible candidates at risk of imminent death from biventricular heart failure. The artificial heart provides circulatory support for the hospitalized patients who are awaiting heart transplantation. The device also improves kidney and liver functions because normal blood flow is restored—making the patient a better candidate for heart transplantation.

TEMPORARILY IMPROVING INSUFFICIENT BLOOD FLOW TO THE BRAIN
http://www.fda.gov/cdrh/mda/docs/h030005.html
The NeuroFlo™ Catheter, manufactured by CoAxia, Inc., is used to treat cerebral ischemia, insufficient blood flow to the brain, resulting from symptomatic vasospasm. Symptomatic vasospasm, the squeezing down of a blood vessel in the brain, results in symptoms similar to stroke such as difficulty in speaking, movement, or understanding. The NeuroFlo Catheter is intended to increase blood flow to the upper body and brain by temporarily reducing blood flow to the lower part of the body.

MDUFMA

FDA worked to implement the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. MDUFMA allows CDRH to collect user fees from companies that submit medical device applications. CDRH has used the additional funds to hire additional staff expertise and develop better systems to support more effective and timely review.

MDUFMA requires CDRH to pursue a complex and comprehensive set of review goals that are more aggressive each successive year. CDRH reports on performance relative to the specified goals at the end of each year. In FY 2005 CDRH fulfilled MDUFMA statutory requirements and maintained device review performance in areas not covered by official performance goals. Enactment of the Medical Device User Fee Stabilization Act of 2005 provided the final action necessary to satisfy the Committee's request for

"updates on the progress of the MDUFMA legislative change." The Stabilization Act enabled the legislative changes required to continue the medical device user fee law through FY 2007. Information about MDUFMA is available at http://www.fda.gov/cdrh/mdufma/index.html.

DOCUMENTS, NOTICES AND REPORTS RELATED TO MDUFMA

In FY 2005 CDRH published three *Federal Register* notices about MDUFMA implementation. In addition, for FY 2005, CDRH prepared three reports to Congress related to MDUFMA:

- Annual Report to Congress on the Office of Combination Products for FY 2005
- Annual Financial Report to Congress –for FY 2005
- Annual Performance Report to Congress –for FY 2005

THIRD PARTY INSPECTION PROGRAM

http://www.fda.gov/cdrh/ap-inspection/ap-inspection.html

CDRH continued implementation of the MDUFMA Accredited Persons (APs - Third Party inspection) program designed to reduce regulatory burden on providers, patients, and consumers of health and human services by increasing efficiency and modernizing regulatory oversight. During FY 2005 the number of qualifying inspections for APs increased by 10 percent. Currently, 5 of 16 APs are eligible to conduct independent inspections for the FDA. In a letter to 8,600 domestic Class II and Class III device establishments, CDRH announced the publication of the AP Eligibility Guidance and outlined the benefits to manufacturers who use an AP to conduct their AP inspections.

MDUFMA STAKEHOLDERS ANNUAL MEETING

http://www.fda.gov/cdrh/meetings/111804.html

CDRH held the 2nd Annual Stakeholder Meeting on the Implementation of MDUFMA on November 18, 2004. This meeting addressed FDA's progress in implementing the various MDUFMA provisions, including the guidance documents FDA issued under the new law. The meeting gave stakeholders an opportunity to provide information and share their views on the implementation of MDUFMA.

SMALL BUSINESS DETERMINATIONS (SBD)

http://www.fda.gov/cdrh/mdufma/guidance/

Firms that qualify as MDUFMA small businesses are eligible to pay reduced fees for medical device applications that are subject to a user fee. In FY 2005 CDRH received, evaluated, and responded to 674 requests for Small Business Determinations under the meaning of MDUFMA, and granted 644, an increase of 13 percent over FY 2004.

INCREASING ACCESS TO INNOVATIVE TECHNOLOGIES

MDUFMA PERFORMANCE

CDRH made steady progress in developing and deploying process improvements in its medical device review program. The Center set milestones for measuring review progress more frequently and for tracking each PMA individually. Quarterly progress updates are available on the MDUFMA web site at http://www.fda.gov/cdrh/mdufma/index.html.

TRAINING AND PROFESSIONAL DEVELOPMENT

CDRH is committed to strengthening its workforce. CDRH's Staff College provides employees with comprehensive professional and technical training through classroom training, live satellite teleconferences, web casts, online coursework, and a variety of seminars and lectures. In FY 2005 CDRH increased to 37 the number of technical science courses available to staff and improved its new employee training and reviewer training. In total, 852 employees enrolled in 153 different courses. The Center also made significant advances toward developing science, management and business competency models.

GUIDANCE DEVELOPMENT

http://www.fda.gov/cdrh/mdufma/guidance/

Guidance development facilitates interactions with industry and ensures effective program implementation. CDRH issued guidance documents on premarket approval applications, premarket assessment of pediatric medical devices, and premarket assessment and use of validation data for reprocessed single use devices. In total, CDRH issued 28 guidance documents in FY 2005.

UTILIZING EXTERNAL EXPERTISE

CDRH ADVISORY COMMITTEES

http://www.fda.gov/cdrh/panel/

CDRH held 17 Federal Advisory Committee panel meetings in 2005. These panels of external experts reviewed and made recommendations to FDA on 10 premarket approval (PMA) applications, one humanitarian device exemption (HDE), two premarket notifications (510(k)s), five pre-amendment device classifications, and six general issues. Among the topics addressed at the meetings were issues associated with significant breakthrough technologies for endovascular aortic repair, blood vessels connection, and hip joint resurfacing.

INCREASING ACCESS TO INNOVATIVE TECHNOLOGIES

MEDICAL DEVICE FELLOWSHIP PROGRAM (MDFP)
http://www.fda.gov/cdrh/mdfp/about.html
CDRH established the Medical Device Fellowship Program (MDFP) to increase the range and depth of collaborations between CDRH and the outside scientific community. The MDFP offers short and long-term fellowship opportunities for individuals interested in learning about the regulatory process and sharing their knowledge and experience with medical devices from the relatively simple to the highly complex. In FY 2005 MDFP worked with National Research Council Associates Program on a Resident Research Associateship Program, and on a memorandum of understanding (MOU) with Duke University and Brigham and Women's Hospital. MDFP programs provide doctoral scientists and engineers of unusual ability and promise or proven achievement with an opportunity to conduct research on problems which are compatible with CDRH research and review interest.

By the end of FY 2005 CDRH had brought in 74 new experts under the Medical Device Fellowship Program (MDFP). These included engineers, medical officers, statisticians, scientists, project managers, consumer safety officers, and program support staff to increase CDRH's scientific and technical capabilities.

THIRD PARTY REVIEW PROGRAM
http://www.fda.gov/cdrh/thirdparty/index.html
The Accredited Persons Program was created by the FDA Modernization Act of 1997 (FDAMA), based on an FDA pilot. The purpose of the program is to improve the efficiency and timeliness of FDA's 510(k) process, the process by which most medical devices receive marketing clearance in the United States. Under the program, FDA has accredited third parties (Accredited Persons) that are authorized to conduct the primary review of 510(k)s for eligible devices. Persons who are required to submit 510(k)s for these devices may elect to contract with an Accredited Person and submit a 510(k) directly to the Accredited Person. The Accredited Person conducts the primary review of the 510(k), then forwards its review, recommendation, and the 510(k) to FDA. By law, FDA must issue a final determination within 30 days after receiving the recommendation of an Accredited Person. Submitters of 510(k)s who do not wish to use an Accredited Person may submit their 510(k)s directly to FDA.

In FY 2005 FDA increased the use of the Third Party Review Program for 510(k) submissions. CDRH received 243 510(k) submissions, which were reviewed by third party organizations under the Accredited Persons provisions (section 523) of the Federal Food, Drug, and Cosmetic Act. The program realized a 27 percent increase since FY 2003. The Center made final decisions on 251 third party 510(k) submissions, an increase from the 244 final decisions in FY 2004. CDRH continued to improve the quality and consistency of third party reviews and facilitate timely action on these submissions. In FY 2005 CDRH conducted a training session for FDA staff and for third party reviewers. In addition, telephone conferences with all third parties in January and April 2005 provided a routine forum for discussing issues and answering questions.

INCREASING ACCESS TO INNOVATIVE TECHNOLOGIES

MAINTAINING THE QUALITY OF PREMARKET REVIEWS

CDRH QUALITY REVIEW PROGRAM

CDRH's quality review program for premarket submissions evaluates the quality of its scientific review. The program started by focusing on three key areas:

- biocompatibility
- sterilization
- statistical analysis.

The Center has initiated improvements in reviewer training in these areas, based on the findings of this program. Other review areas will soon be added to the program, including software and clinical protocol reviews. This on-going process will allow CDRH to improve the quality of its reviews in key scientific areas, thus ensuring that reviewers consistently ask the right questions at the right times.

IMPROVING PROBLEM DETECTION

CDRH is taking steps to increase its ability to identify, analyze, and act on postmarket information to improve the safety and effectiveness of medical devices and radiation-emitting products. In FY 2005 the Center overtook a comprehensive inventory of its postmarket safety programs, made changes to the condition of approval program and in collaboration with the industry and professional association worked to improve adverse event detection and management.

IMPROVING POSTMARKET SURVEILLANCE

MEDICAL DEVICE POSTMARKET TRANSFORMATION INITIATIVE

http://www.fda.gov/cdrh/postmarket/mdpi.html

In FY 2005 CDRH overtook a comprehensive inventory of its postmarket safety programs, including recalls, MDR and MedSun. In each of these areas, the Center looked at its successes and challenges in implementing an effective program. The postmarket safety program inventory considered how the Center identifies postmarket problems, assesses the information obtained, and responds to that information through both stakeholder communication and enforcement action. The Center's plan to strengthen its postmarket program focuses on: developing a "culture of collaboration" for postmarket safety within the Center; developing world-class data sources and systems to quickly and accurately collect, analyze, and disseminate information about potential risks; enhancing risk communication efforts; and improving coordination with the FDA field staff. A senior-level team, comprised of CDRH management and outside consultants experienced in medical device safety and product regulation will help guide the Center in this effort.

IMPROVING COORDINATION OF POST-APROVAL STUDIES

The post-approval studies program involves the review, design and tracking of clinical studies that are required of manufacturers as a condition of approval of a PMA. In January 2005 CDRH transferred the coordination of the post-approval studies program to the Office of Device Evaluation to the Office of Surveillance and Biometrics. CDRH worked with sponsors design post-approval studies that answer important postmarket questions and are realistic and founded on good science, developed a guidance document for use by sponsors that specifies reporting requirements, and implemented a tracking system to ensure that studies are timely and accurate and provide useful results that are implemented into revised product labeling.

IMPROVING PROBLEM DETECTION

DEVELOPING A MEDICAL DEVICE ELECTRONIC ADVERSE EVENT REPORTING SYSTEM

CDRH is developing an electronic adverse event reporting system that will facilitate processing the reports and reduce operating costs. In FY 2005 CDRH received, processed, analyzed and responded to about 180,000 medical device adverse events reported through CDRH's Medical Device Reporting (MDR) system. This system uncovered many public health issues and problems ranging from orthodontic headgear, hemodialysis systems and hospital beds, to cochlear implants, deep brain stimulators, and diagnostic tests for heart attacks and pregnancy.

USING TARGETED SURVEILLANCE: THE MEDSUN NETWORK

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/linkwarning/linkwarning.cfm?link=https%3A%2F%2Fwww%2Emedsun%2Enet%2Fabout%2Ehtml

MedSun is CDRH's response to a section of the Food and Drug Administration Modernization Act (FDAMA), which required FDA to move from a mandatory program to surveillance reporting by a subset of clinical facilities. The program's principal objective is to increase both the quantity and quality of user facility reporting by recruiting a cadre of well-trained and motivated facilities, and to establish a collaborative effort to better understand medical device use in the clinical environment. By mid-2005 MedSun expanded to approximately 350 health care institutions (mostly hospitals) nationwide.

In addition to enhancing the detection of emerging device problems, the MedSun network acts as a two-way communication channel between the CDRH and the clinical community and serves as a setting for applied clinical research on device issues. To succeed, the effort must train participants in the recognition and reporting of adverse events, assure reporting confidentiality, minimize the burdens of participation, and provide timely feedback on safety information.

FY 2005 efforts within the network, included:

- MedSun's Annual Conference
- a survey on "single-use device" reprocessing
- development of educational materials
- implementation of the Device Safety Exchange Program (highlighting best safety practices and safety solutions)
- monthly newsletters (highlighting device reports, CDRH actions, and other notable safety initiatives by other agencies)
- clinical engineering audio-conferences
- launching a pilot program for CBER.

IMPROVING PROBLEM DETECTION

MedSun's FY 05 Annual Conference attendees participated in a workshop on infusion pump safety, and received training on problem recognition with laboratory devices and with pediatric devices. A survey evaluation of the current status of "single-use device" reprocessing in the MedSun clinical community was completed. Of the 53 sites participating in this survey, none were aware of any increase in tracked infections in their facility or any deaths or serious injuries associated with the use of reprocessed devices. CDRH developed and made available to MedSun sites educational materials addressing problem recognition and reporting for laboratory devices and devices used on the pediatric population. The Center implemented the Device Safety Exchange (DS-X) Program for online sharing of questions and device quality improvement ideas by MedSun reporting sites. The DS-X web site allows participants to submit questions and ideas directly to MedSun staff who review, edit and post them for view by all MedSun sites. Topics addressed this year included, policies and risks associated with cell phones in the hospital environment and cybersecurity.

CDRH also launched a pilot program for CBER. The program will enable CBER to acquire information from MedSun sites on issues involving human cells and tissues. Engineering audio conferences on this development were provided to all MedSun sites.

DETECTION OF ADVERSE MEDICAL DEVICE EVENTS WITH ELECTRONIC DISCHARGE RECORDS

CDRH began several collaborations with the Agency for Healthcare Research and Quality, which administers several data sets of interest, including the Healthcare Utilization Project Nationwide Inpatient Sample (NIS) of hospital discharge claims and the State Inpatient Databases (SID) of hospital discharge claims. An interagency group used the NIS and SID to study short term health problems among those who had three types of hip prosthesis surgery: total hip replacement, partial hip replacement, and revision of an existing hip prosthesis. Although similar studies have been done with smaller patient groups, this is the first to use a national dataset to make national estimates of the short term outcomes of hip prosthesis surgery. A different team used the NIS data to estimate national numbers of discharges for specific diagnoses of device-related problems. This latter study is the first systematic description of the national burden of adverse medical device events using hospital discharge records. A third project, still in progress, is examining and comparing the data available in NIS and in the CDRH adverse event reports for automatic implantable cardioverter defibrillators.

ACTIVE DEVICE SURVEILLANCE

CDRH continued the contract with the University of Utah for Phase 2 of a pilot on active surveillance of medical device problems in hospitals. The new direct observation portion of the project is meant to establish a "gold standard" estimate of the number of device-related adverse events occurring in a hospital setting. The methodology is to note problems with device use as comprehensively as possible by directly observing patient care and actively soliciting information on adverse device events from as many sources

as feasible. This project builds on the pilot of active surveillance of medical device problems in hospitals.

DATA MINING

CDRH is contracting with Lincoln Technologies in using their web-based safety data mining environment called WebVDME to mine device adverse event data. This software has been used at CDER to study age/gender effects, to predict the safety profiles of proposed combination drugs, and to separate contributions of individual drugs to safety problems in poly-therapy situations. This tool may be a way to optimize evaluation resources and enhance CDRH's ability to identify device-related safety concerns. The use of enhanced data mining techniques may improve upon CDRH's current ability to identify adverse event patterns in postmarket safety databases.

MINIMIZING USER-RELATED HAZARDS

HUMAN FACTORS AND LABELING

http://www.fda.gov/cdrh/humanfactors/whatis.html

Human factors (HF) is the study of how people use technology. It involves the interaction of human abilities, expectations, and limitations, with work environments, and system design. The term "human factors engineering" (HFE) refers to the application of human factors principles to the design of devices and systems. It is often interchanged with the terms "human engineering," "usability engineering," or "ergonomics." The goal of HFE is to design devices that users accept willingly and operate safely in realistic conditions. In medical applications, HFE helps improve human performance and reduce the risks associated with use error.

CDRH's human factors and labeling efforts help minimize use-related hazards, assure that intended users are able to use medical devices safely and effectively, and facilitate reviews of new device submissions. During FY 2005 the Center's human factors and labeling activities included -- performing 84 labeling and 10 human factors reviews, working to apply eLabeling principles to 4 prototypes, and evaluating CDRH's process for incorporating human factors principles into premarket review.

IMPROVING PROBLEM DETECTION

INTERNATIONAL PROGRAMS

GLOBAL HARMONIZATION

This fiscal year, CDRH worked with foreign governments to facilitate international harmonization, specifically under the United States/European Community Mutual Recognition Agreement on transatlantic trade and the Global Harmonization Task Force (GHTF).[1]

The Medical Device Annex of the MRA covers the exchange of quality systems evaluation reports for all medical devices and premarket evaluation reports for selected low to medium risk devices. The Sixth Annual Report of the Medical Devices Annex to the U.S./EC Mutual Recognition Agreement (MRA), a joint report by the FDA, the National Institute of Standards and Technology (NIST) and the Commission for the European Communities (CEC) was issued December 2004. The report addressed the implementation of the Medical Devices Annex and contained accomplishments from December 1, 2003 to December 1, 2004. The report is available at http://www.fda.gov/cdrh/mra/annualreport2004.html.

In September 2005 FDA hosted a GHTF Joint Study Group Meeting. A Joint Study Group Meeting was held to facilitate cross-consultation and joint consideration of issues by the study groups and provide a forum to update the members on the activities of all of the study groups.

[1] GHTF is an international voluntary group of representatives from national medical device regulatory authorities and the regulated industry. The United States is one of the five founding members of GHTF. Members are from the following three geographical areas: Asia, Europe, and North America. The purpose of the GHTF is to encourage convergence in regulatory practices related to ensuring the safety, effectiveness, performance and quality of medical devices; and promoting technological innovation and facilitating international trade. The primary way in which this is accomplished is via the publication and dissemination of harmonized guidance documents on basic regulatory practices. Study groups are responsible for the drafting of the harmonized guidance documents.

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

In FY 2005 CDRH continued to improve communication by providing increased access to information on regulated products and health issues on its FDA web sites, in newsletters, through increased outreach efforts, and through internal operational initiatives. CDRH's web sites offer new and in-depth information on how to get healthy and stay healthy. They also offer information on current CDRH activities to ensure that medical devices and radiation-emitting products are fit to use.

INCREASING ACCESS TO INFORMATION ON REGULATED PRODUCTS AND HEALTH ISSUES

MEDICAL DEVICE RECALL WEB SITE
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/medicaldevicesafety/recalls.cfm
In FY 05 CDRH redesigned the Medical Device Recall web site to provide a web-friendly, plain language overview of medical device recalls. The web site now explains the various classes of medical device recalls and the procedures that FDA and companies follow during a recall. The web site continues to describe each Class I recall in a plain language format and provides access to the new recall database.

PUBLIC HEALTH NOTIFICATIONS
http://www.fda.gov/cdrh/safety.html
Notices, available on the Public Health Notification web site, are issued to mitigate risk from medical device problems. FY 2005 notifications covered issues such as:

- Ralstonia bacteria contamination of a humidifier used in neonates
- Recommendations for clinicians concerning the recalled Enterex implantable device for Gastroesophageal Reflux Disease (GERD)

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

- Information about failures with the Guidant Implantable Cardioverter Defibrillator
- Recommendations to avoid entrapment of vulnerable patients in the Vail bed.

FDA PATIENT SAFETY NEWS (FDA PSN)
http://www.fda.gov/cdrh/psn
CDRH coordinated the agency production of FDA Patient Safety News, an award-winning monthly television news show and web site distributed to health care practitioners across the nation. FDA PSN covers a wide range of stories on medical errors, patient safety, recalls and alerts, and newly approved drugs, devices and biological products. The news show is a major agency vehicle for communicating FDA safety messages on medical products to physicians, nurses and pharmacists. The video feature of the program often improves the understanding of safety issues, particularly in circumstances such as identifying counterfeit drugs, demonstrating how medical errors occur, and depicting recalled products. Because of this, the video program is often used by risk managers and educators to train health care staff on the safe use of drugs, devices, and biologics. In FY 2005 the FDA PSN web site received about 8,500 "hits" per month, an increase of about 40 percent over the previous year.

TOPIC-SPECIFIC WEB SITES

CDRH developed and updated various topic-specific web pages, including those for breast implants and cochlear implants. These sites provide information about high interest topics, including newly approved and first-of-a-kind device technologies. Information in the sites includes questions to discuss with the doctor. Currently, there are eight sites, including a newly launched Phakic Intraocular Lenses web site (http://www.fda.gov/cdrh/phakic/).

FDA & YOU
www.fda.gov/cdrh/fdaandyou/index.html
Now in its second year of online publication, the FDA & You newsletter targets secondary school students and health educators. FDA & You provides information on FDA topics of interest to teenagers.

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

EXPLORING WAYS TO IMPROVE ACCESS TO CDRH'S INFORMATION

SMALL MANUFACTURERS, INTERNATIONAL AND CONSUMER ASSISTANCE
http://www.fda.gov/cdrh/industry/support/
CDRH's Division of Small Manufacturers, International and Consumer Assistance (DSMICA) was mandated by the 1976 medical device legislation to provide technical and regulatory assistance to small manufacturers and help them comply with Food and Drug Administration (FDA) requirements for medical devices.

Through DSMICA and its Device Advice web site (http://www.fda.gov/cdrh/devadvice/), CDRH provides regulatory assistance to medical device manufacturers, consumers and foreign governments. CDRH provides manufacturers assistance with:

- product classification
- premarket and postmarket requirements
- labeling
- manufacturing requirements (quality system)
- import/export issues for medical devices
- reporting requirements for electronic products.

Consumers can obtain information on medical devices and radiation-emitting products that help them enhance their ability to avoid risk, achieve maximum benefit, and make informed decisions about the use of medical devices and radiation-emitting products.

CDRH also identifies and supports international and global harmonization activities, including educating foreign governments on the medical device regulatory process, and directing U.S. firms to sources of information on foreign requirements for medical devices.

In FY 2005 CDRH continued providing assistance and outreach to help small manufacturers and international producers comply with FDA requirements for medical devices. CDRH answered 44,000 requests for information, 7,000 responses involving international activities, and distributed 82,000 guidance documents on inspection and enforcement procedures, product development, and regulatory submissions. CDRH's outreach efforts took the Center to 47 domestic and international manufacturers' meetings, conferences, and workshops.

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

E-CONSUMER INITIATIVE

NEW WEB FEATURES

In FY 2005 several new features were added to the CDRH web site to offer users options regarding how they receive information about medical devices and radiation-emitting products information. New tools included:

- Email subscription management system
- Real Simple Syndication (RSS) feeds

The email subscription service alerts customers when information of interest to them has been added or updated on the web sites. It allows users of the CDRH web site to create profiles of interest by subject area. RSS feeds deliver news directly to a user's desktop. RSS is an XML-based format for sharing and distributing CDRH Web content, including new device approvals, recalls, and other news items.

IMPROVING COMMUNICATION

CDRH uses multiple tools to ensure efficient outreach efforts. In FY 2005 these tools included:

- satisfaction surveys
- program evaluations
- web usability testing
- unsolicited feedback (i.e., letters and phone calls)
- conference participation
- paper media (e.g., newsletters and brochures).

In FY 2005, CDRH conducted an online survey of 1,006 CDRH web site users. CDRH asked user what they needed from its web sites and their satisfaction with the information available. This information will help CDRH improve the services it provides to the public. CDRH also participated in six professional and health educator conferences. At the conferences Center staff provided patient safety information and promoted CDRH communication programs.

CDRH promoted the use of risk communication methodologies throughout the Center raising awareness about the importance of effective communication with internal and external groups. This was accomplished by providing training conducted by expert Risk Communicators and Center Staff.

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

Various easy-to-read health brochures are available to the public through CDRH. This year the CDRH updated its Human Factors, Breast Implant, and Office of In Vitro Diagnostics (OIVD) brochures. These brochures are disseminated through various mechanisms including web, conferences, and professional and industry meetings.

IMPROVING THE COMMUNICATION INFRASTRUCTURE

UNITING PRE AND POSTMARKET: CDRH DEFIBRILLATOR WORKING GROUP
Established in FY 2005 the CDRH Defibrillator Working Group unites both premarket and postmarket working groups with the goal of disseminating relevant information regarding device approvals, adverse events, recalls and other pertinent issues. This working group is an example of the Center's Total Product Life Cycle (TPLC) approach in that the information learned from the postmarket arena can then be used to support premarket reviews.

INFORMATION TECHNOLOGY (IT) SOLUTIONS
CDRH's Information Management Steering Committee (IMSC), whose members are CDRH senior management, began working in FY 2005 towards ensuring that IT projects are consistent with Center strategic goals and priorities, and toward developing a meaningful CDRH IT Strategic Plan. In addition, CDRH began using project management plans, a performance measurement tool, to implement and monitor the progress of major IT projects.

IT systems allow for better monitoring and tracking of premarket submissions and for improved communication and coordination among review teams. CDRH continued using the Center-level premarket tracking system to help monitor and manage CDRH workload to ensure that appropriate scientific expertise is used to review each document. In FY 05 the Center began piloting the use of eRoom, a web-based collaboration tool, in support of Premarket Approval Application reviews. The software allows for real-time information sharing and communication among review team members and provides a central location for document storage and retrieval. Additional FY 2005 projects included:

- tracking system for Conditions of Approval postmarket studies (COATS)
- electronic consultations tracking (eConsult)
- device nomenclature management system (DNMS)
- enhancements to the system for the generation and electronic submittal of in vitro diagnostics (IVD) applications (Turbo510k)
- program for accepting electronic premarket submissions (eCopy)
- program for accepting and processing electronic adverse event reports (eMDR).

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

COLLABORATING TO PROMOTE EFFECTIVE PUBLIC HEALTH COMMUNICATION

The Center's top priority is to increase its ability to obtain critical information about medical device failures and to communicate this information clearly and rapidly to physicians and the public so they can use it to make sound, informed medical decisions.

CDRH maintains cooperative relationships with professional societies and trade organizations to promote effective public health communication. These organizations include the American College of Cardiology; American Dental and American Diabetes Associations; American Association of Pediatrics; American College of Radiology; Conference of Radiation Control Program Directors; AdvaMed; Food and Drug Law Institute, and Medical Device Manufacturers Association.

POLICY CONFERENCE ON IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS) AND PACEMAKERS

http://www.hrsonline.org/uploadDocs/HRS_Device-Performance-Recommendations-Apr06.pdf

The September 2005 Heart Rhythm Society (HRS) policy conference on implantable cardioverter defibrillators and pacemakers was a good step toward improving communications with clinicians, patients, industry representatives, and regulators. The purpose of the conference was to review the current process for recalls and to discuss the important elements of risk communication that can help guide physicians in treating patients with recalled defective devices.

RETROSPECTIVE REVIEW OF PACEMAKERS AND IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICDS)

http://www.fda.gov/bbs/topics/NEWS/2005/NEW01231.html

As part of the agency's ongoing commitment to improve the safety monitoring of ICDs and provide earlier notices to doctors and patients of potential problems, FDA announced its retrospective review (initiated in 2003) of ICD's and pacemakers malfunctions. FDA's findings were released at the September 16, 2005 Heart Rhythm Society (HRS) Policy Conference in Washington, DC.

IMPROVING COMMUNICATION OF MEDICAL TECHNOLOGY INFORMATION

PROMOTING THE SAFE USE OF INFUSION PUMPS

http://www.fda.gov/cdrh/cdrhhhc/ The CDRH Home Health Care Committee is tasked with reviewing what the Center does to address problems when devices are used in the home and recommending further Center actions to assure that devices are being used safely and effectively in the home environment. In FY 05 CDRH continued its efforts to address the needs of the growing number of patients using clinical medical devices in this environment. The Center developed an outreach strategy to promote the safe use of infusion pumps. The Center asked manufacturers of infusion pumps to submit instructions for use and basic pump information for every pump marketed during or after 1984. With this information, the Center developed a prototype electronic repository of manufacturers' infusion pump labels containing pump information and instructions for use. The repository is under review and CDRH continues to receive information from manufacturers. Once collected, the label information will become part of CDRH's publicly accessible home health care device web site. Label availability will increase the likelihood that patients, the families and health care providers will have continuous access to pump information and instructions, helping to ensure safe and effective home use.

EDUCATING HEALTH PROFESIONALS: TROPONIN

http://www.fda.gov/cdrh/oivd/labsafetytips.html#tip10

The laboratory safety tip was posted by the Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD) on its web page. It is a follow-up to a signal identified from MDR reports and literature on falsely elevated results for Troponin, an indicator test for heart attack. CDRH worked with industry to address this educational need. AdvaMed, a trade association representing medical device manufacturers, drafted the tip in response to concerns about this issue expressed by FDA.

BUILDING QUALITY INTO DEVICE CLINICAL TRIALS WORKSHOP

In FY 2005, the CDRH Bioresearch Monitoring Group collaborated with the Food and Drug Law Institute (FDLI) to improve the quality of device clinical trials by using a "Best Practices" approach. CDRH developed and presented a workshop for the domestic and international industry entitled "Integrating Quality into Device Clinical Trials". The telecast reached 115 US and international sites with approximately 1000 attendees.

510(K) WORKSHOP FOR NEW MANUFACTURERS

CDRH worked collaboratively with members of industry to host a workshop on 510(k) submissions at the annual meeting of the Association of Medical Device Manufacturers. The workshop helped companies new to the *in vitro* diagnostics industry learn how to develop and submit high quality 510(k) submissions. Both CDRH and industry believe that helping companies understand good trial design and how to develop submissions

conforming to CDRH administrative and scientific requirements will produce more reliable and rapid reviews which will benefit device manufacturers and the public.

FDA MEDICAL DEVICE WORKSHOP

In September 2005 CDRH and FDA Los Angeles District Office conducted a FDA medical device three workshops in Los Angeles, CA. The three-day event consisted of a one-day workshop each day. The three topics addressed were:

- Premarket Requirements
- Quality System Requirements
- CDRH's Office of In Vitro Diagnostic Device (OIVD) Evaluation and Safety.
-
- Over 4,000 FDA registered establishments in the Los Angeles district were invited to attend these workshops. Registration is limited to 200 attendees per workshop-day. There was no registration fee for attendees to these workshops.

WORKSHOP ON DRUG-DIAGNOSTICS TRANSLATIONAL RESEARCH

The new field of pharmacogenetic research will enable pharmaceutical companies to develop drug treatments that precisely target the needs of particular patient populations. By linking drug treatments to diagnostic tests that can accurately identify appropriate receptive patients, pharmaceutical companies aim to decrease drug adverse events, increase drug response rates, and ultimately save healthcare dollars. In April 2005 CDRH held the third in a series of national workshops on drug and diagnostic co-development. The workshop gave stakeholders a public venue for scientific suggestions and concerns about FDA regulatory practices in this important and growing new area. CDRH is using the proceedings of this conference to develop guidance to ensure that this research translates in a rapid and cost-effective manner to new joint products that can quickly enter the medical marketplace.

USING RISK INFORMATION TO PROTECT THE PUBLIC

PROTECTING HUMAN RESEARCH SUBJECTS AND CONFRONTING RESEARCH MISCONDUCT

The Bioresearch Monitoring (BIMO) program is entrusted with protecting the rights, safety, and welfare of human research subjects and insuring the quality and integrity of device research.

APPLICATION OF INTEGRITY POLICY

Implementation of FDA's Application Integrity Policy involves investigations of sponsors that are suspected of submitting false or misleading data to the FDA. It also includes the review, evaluation, and monitoring of validity assessments required to be completed by sponsors found guilty of fraudulent activities. In FY 2005 CDRH invoked the Application Integrity Policy (AIP) against a manufacturer and a distributor of drugs of abuse test kits. This action effectively removed thousands of potentially inaccurate and ineffective diagnostic drugs of abuse test kits from the marketplace. Because of this action, CDRH suspended the substantive review of eight of the manufacturer's pending 510(k) marketing submissions, and the manufacturer subsequently withdrew 18 additional cleared 510(k) marketing submissions due to widespread data inconsistencies and questionable design and research practices.

REMOVAL FROM THE APPLICATION INTEGRITY POLICY LIST AND THE INTEGRITY HOLD LIST

The Application Integrity Policy is invoked in cases where unreliable safety or effectiveness data is uncovered in numerous applications currently under FDA review and evaluation while the Integrity Hold is invoked when questionable data is uncovered in only one application under FDA review. In FY 2005, CDRH removed one sponsor from the AIP list and three sponsors from the integrity hold list. Removal from both lists are based upon the sponsor's successful implementation of a corrective action plan that addresses shortcomings in the oversight of device research and assures higher quality marketing submissions.

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDING AND OPPORTUNITY TO EXPLAIN LETTERS (NIDPOE)

A NIDPOE letter informs the recipient clinical investigator that FDA is initiating an administrative proceeding to determine whether the clinical investigator should be disqualified from receiving investigational products pursuant to the Food and Drug Administration's regulations. Generally, FDA issues a NIDPOE letter when it believes it has evidence that the clinical investigator repeatedly or deliberately violated FDA's regulations governing the proper conduct of clinical studies involving investigational products or submitted false information to the sponsor. In FY 2005 CDRH issued two NIDPOE letters to clinical investigators, one of which resulted in a restricted agreement between the Agency and the clinical investigator.

INSTITUTIONAL REVIEW BOARDS (IRBS) FAILURE TO IMPLEMENT CORRECTIVE ACTIONS RESULTED IN FDA WITHHOLDING APPORVAL OF NEW STUDIES

In FY 2005 CDRH issued Warning Letters to two IRBs for continuing to fail to comply with FDA regulations applicable to IRBs. The Warning Letters were issued following inspections whose purpose was to determine if the IRBs had implemented corrective actions assured in their response to previous Warning Letters and to determine if the IRBs were presently functioning in compliance with applicable FDA regulations. The Warning Letters requested that the IRBs take immediate action to correct the violations. Furthermore, the Warning Letters notified the IRBs that as a continued result of their noncompliance, FDA would withhold approval of new studies reviewed by the IRBs, and that no new subjects could be admitted to ongoing studies that were currently under review by the IRBs. These restrictions would remain in effect until the FDA notified them in writing that their corrective actions were satisfactory.

CDRH BIMO INSPECTIONS
Fiscal Years 2001- 2005

Inspected Entity	2001	2002	2004	2005
Sponsor	50	72	73	70
CI	122	151	183	183
IRB	40	128	73	48
GLP	2	6	19	31

Figure 1. *BIMO Warning Letters by Year*

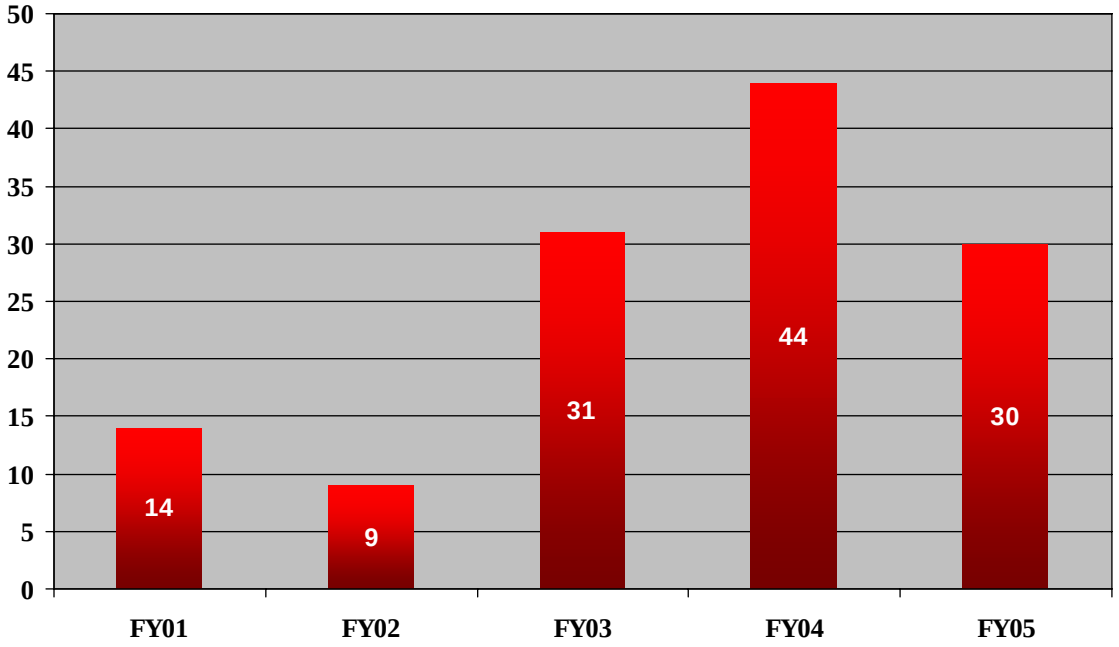
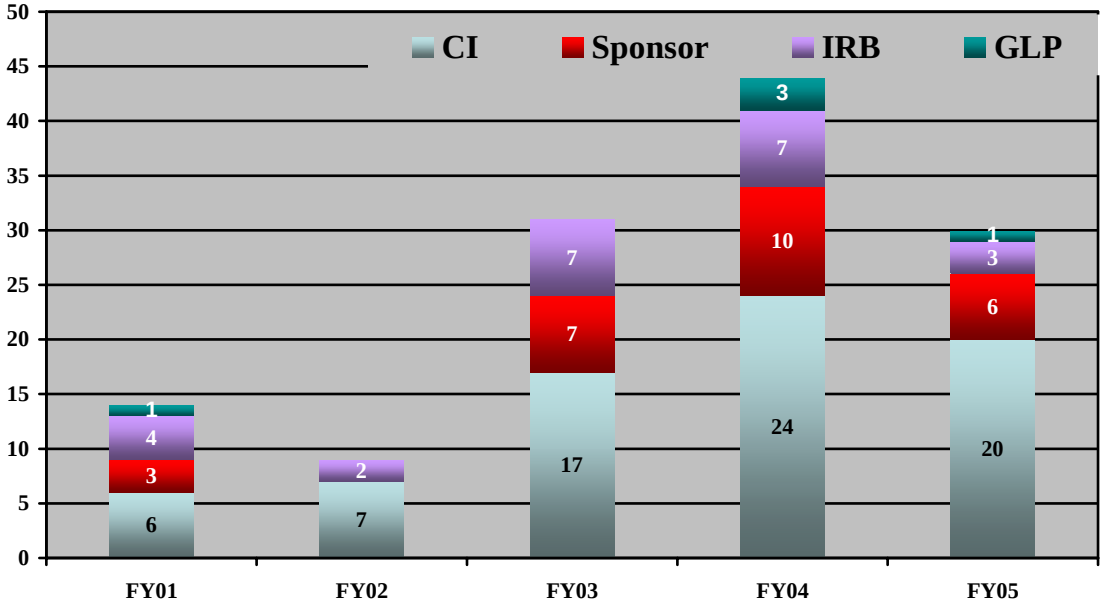


Figure 2. *BIMO Warning Letters by Year and Type*



USING RISK INFORMATION TO PROTECT THE PUBLIC

IMPROVING PRODUCT QUALITY AND SAFETY THROUGH BETTER MANUFACTURING OVERSIGHT

DEVELOPING A COMPLIANCE AND ENFORCEMENT TRACKING SYSTEM
In FY 2005 CDRH's Office of Compliance developed and received approval for the Vision Document, the initial phase in developing the compliance and enforcement component to the Center Tracking system (CTS), a work flow and work management system. The new CTS component will provide better tracking of regulatory actions and their outcomes. CDRH also participated in the requirements analysis for new and improved agency IT systems that will ensure that data collected will be meaningful and provide the data necessary for distributing resources and making risk-based prioritization schemes.

PROTECTING THE PUBLIC
http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/medicaldevicesafety/recalls.cfm
CDRH completed several administrative and judicial actions to protect the American public. In FY 05, CDRH processed:

- 182 warning letters
- 571 product recalls, including 25 highest-risk Class I, 423 Class II, and 123 Class III recalls

PRIORITIZING COMPLIANCE-RELATED ACTIVITIES

CDRH continued to formulate a risk-based management program for inspection and enforcement actions. This process improves the decisions CDRH makes in regulating and monitoring the medical device industry. It not only impacts how inspections are prioritized, but will help to identify and prioritize other types of regulatory activities, such as device recalls, that present the greatest risk to public health.

RISK-BASEB INSPECTION WORK-PLAN AND REGULATORY ACTIONS
In FY 2005 CDRH continued using the inclusive risk-based inspection work plan process. This process ensures that all Center program offices have an opportunity to provide input into the prioritization of special emphasis inspections.

In addition, CDRH analyzed 132 Warning Letters previously issued to medical device manufacturers. In the analysis, CDRH found that 75 percent of the citations related to

GMP violations and 24 percent related to MDR violations. This information also helped making decisions on inspection priorities and regulatory actions.

EXCEEDING YEARLY INSPECTION GOALS

CDRH coordinated with the Office of Regulatory Affairs (ORA) and provided technical support, as necessary, for inspections. In FY 2005 FDA surpassed all CDRH fiscal year inspection goals. FDA conducted:

- 1,265 inspections of registered domestic Class II and Class III medical device manufacturers, exceeding the goal of the goal of 20 percent of the 5,520 registered manufactures
- 230 foreign inspections, exceeding the goal of 7 percent of 2,500 registered foreign Class II and Class III medical device manufacturers
- 335 BIMO inspections with an emphasis on scientific misconduct, data integrity, innovative products, and vulnerable populations, again exceeding its goal of 295 domestic and foreign BIMO inspections.

CLINICAL LABORATORIES IMPROVEMENTS ACT (CLIA)

CLIA established quality standards for all laboratory testing to ensure accurate, reliable and timely patient test results regardless of where a test was performed. Of central importance to the CLIA program is the assignment of a complexity category to commercially marketed diagnostic tests. The tests are categorized into one of three CLIA regulatory categories based on their complexity (i.e., potential risk to public health) and laboratories may only purchase and use a particular test based on the laboratory's level of CLIA certification.

STREAMLINING THE CLIA APPLICATION PROCESSS

Since CDRH reviews the premarket applications for these tests, streamlining the CLIA application process necessitates a transfer of responsibility for complexity determinations from the Center for Disease Control and Prevention (CDC) to FDA. During 2004 FDA completed the delegation of authority to FDA (CDRH) for CLIA complexity determinations and finalized a 5-year Interagency Agreement with the Centers for Medicare and Medicaid Services (CMS) for CLIA waiver authority. In 2005 FDA published draft guidance for the waiver process. The agency is reviewing the comments received in response to the guidance.

USING RISK INFORMATION TO PROTECT THE PUBLIC

MAMMOGRAPHY QUALITY STANDARDS ACT (MQSA)

MQSA FACILITY INSPECTIONS
CDRH conducted annual inspections of over 9,000 mammography facilities nationwide. The Center ensured that 98 percent of mammography facilities met inspection standards. Less than 2 percent of the facilities inspected had level 1 problems. CDRH worked with each of those facilities to assure adequate corrective action is taken.

10 YEARS OF MQSA INSPECTIONS
In FY 2005 CDRH commemorated 10 years of MQSA inspections. So far, MQSA inspectors have completed 93,000 facility inspections nationwide. The percent of inspections without adverse observations has more than doubled in that time, and the trend continues to rise.

RADIATION SAFETY

RADIOLOGICAL HEALTH IMPLEMENTATION PROGRAM
The CDRH Radiological Health Implementation Program Core Group was commissioned in Spring 2005 to consider all previous radiation health program studies and make recommendations for the program's future. Radiological Health activities are critical to providing expertise for the review and approval of treatment and therapy systems, for the prevention of excessive radiation exposures from diagnostics examinations such as fluoroscopy, and for monitoring and evaluation of radiation emitting products such as security screening devices. The recommendations are included in a report titled, "The CDRH Radiological Health Program - Adapting to Current Public Health Needs - 2005–2010," available at http://www.fda.gov/cdrh/radhlth/initiative.html. The new direction of the radiological health program will increase its relevance to, and impact on, the most pressing current public health problems in the radiological health arena and anticipate the evolution of medical radiation systems. FY 2006 efforts will shift to implementing the recommendations.

REDUCING UNNECESSARY EXPOSURE FROM SOURCES REGULATED BY FDA
In the Fall of 2005 CDRH held a meeting to provide a wide range of organizations involved in radiological health an opportunity for dialogue about collective efforts to reduce unnecessary exposure from sources regulated by FDA.

AMENDING GLOBAL LASER REGULATION

CDRH proposed amendments to the Federal Laser Performance Standards, 21 CFR 1040.10 and 1040.100, which adopt by reference and with national exceptions the International Electrotechnical Commission (IEC) laser standards as the new Federal standard. The amendments move to create a single global regulatory environment for laser product manufacturers, reducing the regulatory burden on industry and updating the Federal standard to reflect current laser technology and bioeffects research.

NEW TECHNICAL STANDARDS FOR FLUOROSCOPY EQUIPMENT

CDRH promulgated amendments to the Federal radiation-safety standard improving the performance of diagnostic x-ray systems and their major components. The amended technical standards, published as a final rule in the *Federal Register* on June 10, 2005, will require a number of new equipment features that will significantly reduce unnecessary exposure to x-rays, especially in fluoroscopy, while maintaining the level of image quality requisite for diagnostic efficacy. All fluoroscopic equipment manufactured on or after June 10, 2006, will be required to display values of the rate, duration, and cumulative amount of radiation emissions, thereby enabling a fluoroscopist to adjust techniques in real time to reduce patient exposure. Over the decade following implementation of this final rule, the expected improvement in the quality of health care is projected to reduce the annual U.S. population dose by more than 7,000 person-sievert.[2] The dose reduction could decrease annual cancer deaths by over 200 and create annual savings of over $300 million.

PROMOTING DEVELOPMENT OF CONSISTENT POLICIES ON REDUCING EXPOSURE TO THE GENERAL PUBLIC

CDRH served on the Interagency Steering Committee on Radiation Standards (ISCOR), and in this capacity, promoted development of consistent policies on reducing exposure to the general public. Efforts included recommendations for appropriate use of security products and medical imaging equipment that exposes the public to ionizing radiation.

[2] A sievert (Sv) is a unit of radiation dose equivalent. It replaces the rem (1 Sv equals 100 rem). Some types of radiation do more damage than others for the same absorbed dose – for example, an absorbed dose of alpha radiation causes 20 times as much biological damage as the same dose of beta radiation. The equivalent dose in sieverts is equal to the absorbed dose of radiation in grays multiplied by the relative biological effectiveness.

USING RISK INFORMATION TO PROTECT THE PUBLIC

ASSESSING THE IMPACT OF LEGAL AND ILLEGAL USE OF RADIATION-EMITTING PRODUCTS

CDRH performed an assessment of the impact of legal and illegal use of radiation-emitting products in response to reports of green lasers directed at aircraft with the intent of distracting or temporarily flash-blinding the crew. FDA briefed House Science Committee staff in January 2005 on its authorities regarding the manufacture and use of laser products. FDA worked with the Federal Aviation Administration (FAA), Department of Homeland Security (DHS) and Department of Defense (DoD) to address this problem by providing technical consults in developing aircraft and pilot protective measures. FDA published and contributed to public information regarding safe use of laser pointers and cautioned against internet sales of laser products through various print media outlets and on the Internet. FDA took action against firms that sell modified green lasers that emit radiation in excess of the limit for general public use.

RADIOLOGICAL HEALTH CIVIL MONEY PENALTY ASSESSED AGAINST A MANUFACTURER OF TELEVISION PRODUCTS

In FY 2005 ADI Corporation agreed to pay the second installment of the Radiological Health Civil Money Penalty consent decree for $200,000 by August 2005. The total fine of $475,000 was filed against ADI in May 2003 for unlawful importation of certified television products when the ADI quality control testing program was disapproved. This was the first Radiological Health Civil Money Penalty assessed against a manufacturer of television products.

EXPANDING PATIENT PROTECTION THROUGH APPLIED RESEARCH

CDRH research contributes to the internal review process as well as to the development of guidance for industry in the development of innovative technologies. FY 2005 areas of activity included:

- Device safety in Magnetic Resonance Imaging (MRI) environments
- Expiration date for medical gloves
- Mechanical strength of vertebrae following injections with bone glue
- Exposure to electromagnetic fields and its effects on implanted devices
- Effectiveness and safety of Intraocular lenses (IOLs)
- Combined approach to evaluate circulatory assist devices
- Effects of optical energy
- Device-tissue interfaces
- Better animal models and improved biomarkers

- Reuse of single use devices
- Drug eluting stents
- Modeling to propose design changes to left ventricular assist device
- Computer assisted diagnostic systems
- Performance testing of pulse oximeters
- Test methods for high intensity focused ultrasound
- CDRH standards program

DEVICE SAFETY IN MAGNETIC RESONANCE IMAGING (MRI) ENVIRONMENTS

CDRH developed a new standard practice for marking medical devices and other items safe in the Magnetic Resonance environment. The revised system replaced the old system whose confusing MRI compatible terminology may have resulted in patient injuries.

EXPIRATION DATE FOR MEDICAL GLOVES

CDRH developed and validated a method for assigning an accurate expiration date for medical gloves. This work is critical to protect patients as well as health care workers from the transmission of infectious diseases or agents used in terrorist activities.

MECHANICAL STRENGTH OF VERTEBRAE FOLLOWING INJECTIONS WITH BONE GLUE

CDRH conducted research on the improvement in mechanical strength of vertebrae following injections with bone glue. This has become the most common treatment for compression fractures, a condition estimated to eventually affect a quarter of all women over the age of 50. The findings showed that the procedure can be effective if the bone density has not dropped too low.

EXPOSURE TO ELECTROMAGNETIC FIELDS AND ITS EFFECTS ON IMPLANTED DEVICES

CDRH measured and modeled exposure to electromagnetic fields and the effects on implanted devices from hand held and walk through security systems, cellular telephones, hand-held computers, and MRI systems. This research included models of the head for evaluation of cell phone exposure and of pregnant woman models for 9 gestational ages of the fetus for heating during MRI. This effort resulted in the standardization of specific absorption rate (SAR) across multiple systems. Results of this work include:

- Five journal articles and 14 proceedings and other presentations during the past year
- support from the FAA/TSA (for the security system studies)
- establishment of a CRADA to further the virtual family modeling
- participation in CDRH's Epidemiology Grand Rounds on wireless medical devices

Modeling of the heating effects of MRI upon implanted pacemakers, ICDs, neural stimulators, and cardiac stents helped define the parameters for acceptable application of MRI for individuals with these implanted medical devices and has a potentially large impact on public health.

EFFECTIVENESS AND SAFETY OF INTRAOCULAR LENSES (IOLS)

CDRH developed a significantly more accurate and applicable confocal laser method for testing (IOL) diopter power. Precise measurement is critical for evaluating the effectiveness and safety of IOLs, which are implanted during cataract surgery. The test method has been used to evaluate samples of new IOL designs and on IOLs on regulatory hold because of questions about the labeled power. This work resulted in a pending patent, more than 10 proceedings publications and presentations during the past year, and has been submitted to Nature Methods.

COMBINED APPROACH TO EVALUATE CIRCULATORY ASSIST DEVICES

CDRH developed a combined approach of review and laboratory expertise to evaluate proposed 'subtle' design changes to critical components of life-sustaining mechanical circulatory assist devices. Design of the blood path in these devices is critical for avoiding damage to blood components, stroke, and embolism. CDRH's new combined approach for review significantly reduces the review burden while reducing the uncertainty of the evaluations.

EFFECTS OF OPTICAL ENERGY

CDRH evaluated the effects of optical energy on cellular and intracellular structures and components. This resulted in improved understanding of the effects of light on energy production in cells. CDRH developed a new confocal fiber-optic nano-biosensing system that enables measurements at resolutions better than the theoretical half wavelength limit, resulting in work below the 200 nanometer range. This work, supported in part by an interagency agreement with the Air Force Office of Scientific Research, resulted in four journal articles, numerous proceedings and presentations during the past year, and a proposal to the Army's Telemedicine and Advanced Technologies Research Center to evaluate optical methods of stimulation that may enhance the field of neuro-prostheses.

DEVICE-TISSUE INTERFACES

CDRH also worked towards developing a better understanding of the device-tissue interface for optical spectroscopy leading to improvements in the efficiency of spectroscopic methods for minimally invasive disease detection. This area has the potential to improve the detection of mucosal cancers and the monitoring of changes following therapeutic applications. This work resulted in two journal articles and five proceedings published during the past year.

BETTER ANIMAL MODELS AND BIOMARKERS TO IMPROVE PUBLIC HEALTH

CDRH conducted research to stimulate the development of new evaluation tools - biomarkers and clinically-relevant preclinical models - for assessing the safety and efficacy of new medical products. An animal model of subclinical renal insufficiency that was able to detect known nephrotoxicants at doses that were non-toxic in "healthy" control animals was developed and partially validated. The regulatory impact is significant in that adverse effects detected using the disease model would have been missed using healthy animal models typically used to test medical devices. CDRH also evaluated a new kidney toxicity biomarker, kidney injury molecule that can be measured in kidney tissue and urine, and appears to be more sensitive for renal injury detection than traditional clinical markers. The public health impact is significant in that the new biomarker may be useful to identify patients with subtle renal disease at an earlier stage and prevent pathogenesis of renal failure as well as reduce uncertainties in the preclinical assessment of FDA-regulated products.

INFECTION CONTROL: REUSE OF SINGLE USE DEVICES AND CLEANING VALIDATION

CDRH conducted research to develop and validate cleaning and disinfection/sterilization methods to insure no microbial contamination, misdiagnosis due to tissue contamination, and toxicity resulting from residual detergents and disinfection/sterilization agents remaining on the device. CDRH has determined that total organic carbon is an effective marker of residual soil from patients exposed to the devices and residual chemicals used in reprocessing on cleaned devices versus measuring total protein only as an endpoint of cleaning. The research will improve safety of patients exposed to single-use and reuseable medical devices. Protein residual data from CDRH research have provided an endpoint for device reprocessors to meet requirements of supplemental validation submissions for single-use devices, and aided CDRH reviews and inspection functions.

DRUG COATED STENTS: DRUG ELUTING STENTS ASSOCIATED THROMBOSIS

The drug eluting stents have been shown to exhibit late-stent thrombosis which may be mediated by an increased expression of tissue factor (TF) and decreased levels of thrombomodulin in endothelial cells that line the arteries. CDRH research on the treatment of endothelial cells with either rapamycin or paclitaxel resulted in a slight increase in coagulation activity. However, addition of VEGF significantly augmented the coagulation cascade. Coagulation correlated with increased expression of TF in endothelial cells. Thrombomodulin expression was unaffected by either rapamycin or paclitaxel in the presence of VEGF. Data suggest that platelets and rapamycin/taxol may elevate TF expression. However, platelets themselves are not affected by either drug. These results suggest that anti-proliferative drugs exhibit prothrombotic effects which could be potentiated by VEGF. These findings imply that high levels of VEGF in atherosclerotic plaques could potentially contribute to thrombotic effects observed following drug eluting stent implants.

COMPUTATIONAL FLUID DYNAMICS OF LEFT VENTRICULAR ASSIST DEVICE

CDRH laboratory conducted a study to aid in the evaluation of a post-approval study change for a pediatric left ventricular assist device (LVAD). The sponsor proposed to make a change to the blood flow path within the pump that could have adversely affected hemolysis and thrombogenesis in the pump such that patient safety and/or device efficacy could have been compromised. It would have been extremely difficult, if not impossible, to validate the design changes using animal or human data. After discussions and a meeting with FDA staff, the sponsor agreed to provide experimental (flow visualization, hemolysis) and analytical (computational fluid dynamics [CFD]) testing to support the design changes. CDRH experts recommended appropriate CFD models to the sponsors and analyzed the results.

COMPUTER-ASSISTED DIAGNOSTIC SYSTEMS

CDRH scientists have also played a leading role in the development of new models and methods for the assessment of computer-assisted diagnostic systems. The techniques were first developed during our review of digital mammography systems, and have since been extended to the development of systems for breast cancer screening, lung cancer screening, and CT colonoscopy. Having these tools and methods available has greatly assisted developers of these innovative imaging and CAD-assist devices.

PERFORMANCE TESTING OF PULSE OXIMETERS

CDRH scientists and engineers have developed test methods for a range of non-invasive monitoring devices. CDRH laboratory studies on pulse oximeter performance, for example, enabled substantial improvements in the ISO/IEC standard and the CDRH Guidance Document. This testing facilitated the development of a single test protocol for SpO2 accuracy studies, which simplified the premarket evaluation process by unifying the basis for establishing substantial equivalence. The work has established the groundwork to enable the extensions of claims being made for perfusion measurements and established acceptable performance criteria.

TEST METHODS FOR HIGH INTENSITY FOCUSED ULTRASOUND

The lack of standardized methods to assess the acoustic and thermal characteristics of the focused beams has challenged the regulatory review of these devices, especially in the pre-clinical phase, and has been burdensome to the industry. In the past CDRH scientists and engineers have developed measurement instrumentation and computational modeling techniques for characterizing other types of medical ultrasound devices such as diagnostic imaging and therapeutic ultrasound, and this work has resulted in the creation of numerous regulatory guidance and standards documents. This expertise is being used to accelerate the review of submissions for HIFU devices. For example, in a device for the ablation of uterine fibroids, CDRH-developed computational modeling was used to

predict the performance of the device under conditions that would have been difficult to investigate experimentally, thus shortening the review time.

CDRH STANDARDS PROGRAM

The Standards Management Staff develops and manages the standards used for regulatory assessments. The standards staff facilitates the participation of CDRH and other FDA staff in developing standards. In addition, SMS increases the recognition of voluntary consensus standards for medical devices and radiation-emitting electronic products. As part of this responsibility, the staff publishes lists of recognized standards annually and consistently increases the list of available standards. In 2005, CDRH recognized 48 new standards; and in addition, 110 standards were withdrawn and replaced by new versions, incorporated 98 changes to the existing recognized standards, and 14 standards were withdrawn.

REGULATIONS AND GUIDANCE DEVELOPMENT

CDRH's guidance information is available at http://www.fda.gov/cdrh/guidance.html.

In 2005 CDRH worked to streamline guidance development. Center efforts included:

- prioritizing its guidance workload
- establishing performance goals
- developing and implementing tracking mechanisms
- engaging industry stakeholders in the early stages of guidance development
- increasing the use of contract experts.

CDRH issued 28 guidance documents and accomplished its performance goals. Among these documents were four draft guidance documents; several device-specific and special control guidance documents, including a guidance for intravascular stents and a guidance providing clarity on indications for implanted cardioverter defibrillators; and two key cross-cutting guidance documents - Software used in Medical Devices and Format and Content of 510(k) submissions. The latter document will assist manufacturers in the preparation of 510(k) submissions and should lead to more efficient and timely reviews.

CDRH also worked with the Office of General Counsel and the Office of Policy Regulation editorial staff to review and revise the boilerplate Guidance Development Templates for all guidance documents. These templates are available to Center staff on the Center's intranet web site.

USING RISK INFORMATION TO PROTECT THE PUBLIC

In FY 05, CDRH's guidance and regulation staff responded to nine citizen petitions and published sixteen final rules and forty-seven notices.

PREPARING AND RESPONDING TO EMERGENCIES

CDRH made significant progress in this area. The Center routinely consulted with other government agencies on diagnostic and monitoring devices, radiological counter measures and radiation-emitting devices with potential to be used as weapons (e.g., visible lasers) and on radiation safety issues, including preventing unnecessary radiological exposure from security screening products.

CDRH formed a technical work group to address the use and rapid approval of diagnostics issues related to influenza and assisted CDC in making available to the laboratory response network CDC's rapid diagnostic test.

RESPONDING TO HURRICANE KATRINA

In September 2005, as a response to the Hurricane Katrina emergency, CDRH began posting hurricane and emergency-related information in its web site, available at http://www.fda.gov/cdrh/emergency/index.html. CDRH's web site includes information about:

- Disposal of Contaminated Devices
- FDA Offers Advice About Reopening Dialysis Centers After Restoration of Power and Water
- Natural Disasters - Effects on Mammography Facilities
- FDA Offers Tips about Medical Devices and Hurricane Disasters
- FDA Advice for Medical Devices that Require Refrigeration
- FDA Advice About Medical Devices that Have Been Exposed to High Heat and Humidity
- FDA Health and Safety Tips After Hurricanes for Food, Drugs, Biologic Products, and Animal Health

PREPARING AND RESPONDING TO EMERGENCIES

CONTINUATION OF OPERATIONAL PLANNING (COOP)

The Center conducted COOP activities, participated in emergency preparedness exercises, and maintained the database of medical and in vitro diagnostic devices. The database allows quick identification of device manufacturers and available inventories to facilitate identifying potential shortages in medical and in vitro diagnostic devices that may be needed by emergency health care personnel in the acute phase of an emergency or disaster.

CDRH posted information on cleared and approved devices for personal protection on its emergency information web site, www.fda.gov/cdrh/emergency/flu_qa.html. These devices are integral to minimizing the spread of infectious agents, including those used in bioterrorism.

OBTAINING INFORMATION

ANNUAL REPORTS

CDRH Offices and its Ombudsman publish annual reports. These documents are available on the CDRH web site. A comprehensive list of available annual reports can be found at http://www.fda.gov/cdrh/organiz-info.html and at www.FDA.gov/CDRH.

CDRH WEB SITES

Internet addresses are listed in many sections of this report. CDRH encourages readers to visit these web sites and take advantage of the vast amount of information available in them.

www.FDA.Gov/CDRH